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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/643,424	08/19/2003	Joseph P. Fredrick	10020594-1	4523

7590 11/27/2007

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EXAMINER	
GORDON, BRIAN R	

ART UNIT	PAPER NUMBER
1797	

MAIL DATE	DELIVERY MODE
11/27/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/643,424	FREDRICK, JOSEPH P.	
	Examiner	Art Unit	
	Brian R. Gordon	1797	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 September 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-55* is/are pending in the application.

4a) Of the above claim(s) *19-28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,10-18,29-32,35-45,47-49,51-52,54 and 55* is/are rejected.

7)☒ Claim(s) *9,33,34,46,50 and 53* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Arguments

1. Applicant's arguments filed September 10, 2007 have been fully considered but they are not persuasive.

Applicant has amended the claims to incorporate a number of "configure to" phrases. Recitations of an element being "configured to", "adapted to" or "capable of" performing a function is not a positive limitation but only requires the ability to so perform. It does not constitute a limitation in any patentable sense. For example, claim1 recites the housing chamber being configured to retain any fluid. It should be noted the fluid is not positively claimed as an element of the device. As such, it is only required that the structure of a prior art reference be capable of retaining fluid. It is not required that the prior art structure be specifically disclosed as being employed as such. The ability to retain liquid is the only requirement.

Applicant asserts Loeffler et al. does not disclose "an opening in said housing adapted for insertion into said housing chamber of a substrate having a surface comprising an array of chemical compounds."

As noted above "adapted for" phrases are not further structurally limiting. The only structural requirement of the phrase is a housing chamber opening. The remaining portion of the phrase is directed to how the opening is intended to be used with an unclaimed element. The substrate is not positively claimed as element of the device. The substrate is mentioned in the narrative as to how it could possibly be used with the

opening. As such, it is not required that a prior art reference disclose a housing chamber with an opening used for inserting a substrate. Furthermore, there are no dimensions (size restrictions) given for the opening or substrate, therefore one is not precluded from asserting any housing opening would be capable of allowing a substrate to be inserted therethrough.

The substrate is not an element of the device. As such, any limitations of the unclaimed substrate are not considered further limiting of the claim device. Any limitations directed to the fluid are also not further limiting of the structure of the device.

As such arguments directed to the unclaimed substrate (or any other element that is not positively claimed as an element of the device) are not commensurate in scope with the claims.

The Figures of Loeffler clear show an exploded view of the device in which a slide (substrate) is inserted into the device via the opening of the cover forming the housing.

As to McGrath, applicant asserts "there is no teaching or suggestion in McGrath of a fluid separation mechanism that separates fluid from a substrate "in a controlled manner that preserves the integrity of the fluid meniscus at the atmosphere-fluid interface".

It should be noted that the claim does not define what one considers "a controlled manner". Does this mean the liquid is vacuumed or pumped out at specific rate? Does this mean the substrate is lifted out at a certain rate? There are a number of other factors that would also affect whether or not a meniscus of a fluid is affected by in a

removal process. Other factors attributing to such would be the properties of the fluid itself. A highly viscous fluid is less likely to be disturbed that a fluid of less viscosity. On page 16 applicant states the controlled manner is specifically accomplished by having a specific substrate. As recited above the substrate and fluid referenced in the claims are not an elements of the device. The argument is not commensurate in scope with that of the claims. Furthermore, applicant recognizes McGrath teaches sufficient structure for separating fluid from a substrate. There's no indication that the tilting or suction/vacuum force would be such to disturb the meniscus of the fluid or is not of a constant rate of flow. The examiner asserts the fluid separation structure of McGrath is sufficient/cable of meeting the requirements as claimed.

Applicant asserts Takeuchi has no disclosure whatsoever of a fluid separation mechanism that is configured to separate fluid from a substrate "in a controlled manner that preserves the integrity of the fluid meniscus at the atmosphere-fluid interface". The examiner respectfully disagrees. The transport mechanism T is equivalent to the claimed lifting mechanism. The mechanism is structurally capable of being employed to perform as claimed by applicant.

As to claims 17 and 18 the slide of Loeffler, is disclosed as having an area containing the tissue, biologic cells, or array mounted thereon (column 3, line 20).

As to claim new claim 47, it should be noted a structure capable of performing as that required in claim 1, would be considered to meet the limitations of claim 47.

Claims 3-7, all recite "said controller manner". The claims refer to a single controlled manner. The manner of claim 4 is no different than the manner of claim 3.

The manner in claims 6-7 is no different than that of claim 5. The "controlled manner" is not a further structure of the device but is directed to a functional capability of the device. As given herein, the prior art is capable of functioning in such controlled manner as required by claim 1.

Claim 12, does not add any additional structure but is directed to an intended use. The claim describes how one intends for the separator to be used with an unclaimed "sandwich of a substrate and cover slide". While coverslipping devices are well known in the art, the examiner asserts the clamping system of Loeffler is sufficient to provide for allowing a cover slip to be removed.

New claims 48-53 are not further structurally limiting of the separator mechanism, separator, or wedge of claims 12, 45, and 46 respectively. The claims do not add any additional structure but are directed to the further intended use of the respective elements.

As to claim 29, as stated above there is no indication as to what defines a "controlled manner". Furthermore, there is no indication what velocity rate would or would not be sufficient to eliminate the droplets.

Claim 31 is rejected for the same reason as those recited above in relationship to McGrath. Claim 32 is directed to a Markush group. The references clearly disclose the use of a pump.

In view of applicant's arguments the rejections of claims 9, 33-34, and 46 are hereby withdrawn.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

While its recited the mechanism is for separating fluid from contact with the substrate, no fluid is claimed as being present with contact with the substrate unclaimed substrate. The substrate must be positively claimed as an element of the device.

4. Claim 1 recites the limitation "the fluid meniscus" and "the atmosphere-fluid interface" in (c). There is insufficient antecedent basis for this limitation in the claim. It was not previously established that a fluid is present in the device and the fluid has a meniscus. Where is the fluid and meniscus thereof located. Is the substrate submerged in a fluid in the chamber? Does a layer, film, etc. of fluid coated on all surfaces of the substrate?

5. Claim 1 recites the limitation "the atmosphere-fluid interface" in (c). There is insufficient antecedent basis for this limitation in the claim. It is not inherent that fluid within a housing would have such an interface or be exposed to the atmosphere.

Claim Rejections - 35 USC § 102

6. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

7. Claims 1, 5-8, 10-12, 15-18, 29-30, 32, 36, 45, 47-48, 51, and 54-55 are rejected under 35 U.S.C. 102(e) as being anticipated by Loeffler et al. US 6,673,620.

Loeffler et al. disclose a sample chamber is formed by a housing sealed against a microscope slide. The housing has fluid ports, including a well formed over at least one port. In a rinse station, rinse solution is drawn from a reservoir through the chamber to a waste reservoir. At a fill station, an aliquot of reagent already placed in the well is driven into the chamber. The reagent may be driven into the chamber by first drawing a vacuum on the chamber through the aliquot of reagent and then releasing the reagent to be drawn into the chamber by the vacuum (abstract).

In embodiments of the present invention, a fluid handling apparatus is capable of spreading small amounts of liquid reagent over a flat surface, such as a microscope glass slide. The reagent may be sealed within a confined cavity, or "chamber", so as to prevent evaporation even with heating of small amounts of reagent during an incubation period. One surface of this chamber is the flat slide surface. The remaining surfaces are formed by a cell. The cell is preferably a plastic disposable part that fits on top of the slide, over the area containing the tissue, biologic cells, or array mounted on the glass slide. The cell forms a fluid seal to the surface of the glass by means of a gasket. The gasket is mounted in a recess on the face of the cell that mates with the glass slide.

In another method of fluid injection, reagent is placed into the reagent well, as before. A fluid injector is positioned above the fluid inlet port. In addition, the fluid aspirator is positioned above the fluid outlet port. The valves of both fluid ports are opened by this process. Reagent is then pushed into the chamber by a burst of air

pressure. The transient, high-pressure reagent injection avoids entrapping bubbles by forcing laminar flow of reagent through the chamber. Once the reagent completely fills the chamber, the pressure is removed and the valves are closed by disengaging the fluid injector and fluid aspirator.

Thus, in accordance with one aspect of the invention, an apparatus (fluid separation mechanism) for adding and removing liquid reagents to and from a sample comprises a flat surface supporting the sample and a chamber forming a cavity on the flat surface, the chamber being releasably sealed to the flat surface. Fluids can be added or removed through a fluid port in the wall of the chamber. A source of negative or positive air pressure is provided in a conduit, and an actuator is able to move the fluid port and conduit relative to each other to engage the conduit and fluid ports to each other so that the two are in fluid communication.

FIG. 11 is a perspective representation of an instrument 43 that incorporates positions for eight slides. The instrument 43 is shown with ISH cells in each of the eight positions. Each of the hinged covers 17 is clamped downwards underneath the latch 15. A heater controller pad 45 is located on the front panel of the instrument 43. The heater controller (temperature controller) pad allows someone using the instrument 43 to enter a desired temperature to which the heaters will be heated.

8. Claims 1-8, 10, 16-18,, 29-36, 45, 47, 49, 52, and 54-55 are rejected under 35 U.S.C. 102(b) as being anticipated by McGrath et al. US 5,192,503.

McGrath et al. discloses an automated assay analysis method and a probe clip for in situ assay of tissue sections in the form of a plate having a first seal member

mounted thereon and forming an interior cavity on the plate. In one embodiment, a second seal member is mounted interiorly of the first seal member and divides the interior cavity into first and second fluid communicatable surfaces, with a probe dryingly attached to the plate and disposed on the second mixing surface. The plate is joined to a slide carrying a tissue section and a reactant fluid such to form fluid communicatable reaction and mixing chambers. Successive rotations of the joined plate and slide causes the reactant fluid to initially flow to the mixing chamber and release the probe, before the probe flows to the reaction chamber for reaction with the tissue section. In another embodiment, a time-release material covers the probe mounted on a plate having a single chamber. The reactant fluid hydrolyzes the time-release material to release the probe for reaction with the tissue. The cassette carrying one or more plates is slidingly insertable into a semi-closed housing containing one or more tissue-carrying slides. Clamps urge the probe clip cassette and the individual plates into engagement with the slides to form the sealed chambers therebetween. Inlet and outlet wash ports communicate with the slides to wash the slides after the plates have been removed from the housing (abstract).

The wash means includes an inlet port 178 and an outlet port 180 associated with each receptacle in the case 73, as shown in FIG. 3 and in greater detail in FIG. 9. Each inlet port 178 and outlet port 180 extends through the front wall 130 of the case 73. The inlet port 178 comprises a hollow tube or conduit which opens into the interior of the case 73 in each receptacle. The inlet port 178 is positioned below the slide support members 152 mounted on the base of the case 73. The slide support members 152

extend above the bottom of the case 73 and define a chamber 176 below the slide 50 mounted on the slide support members 152.

The outlet port 180 is connected to a conduit 182 which extends through the case 73 and terminates adjacent the back wall 128. The terminal end of the conduit 182 opens to the interior of the case 73 in the receptacle so as to receive fluid from above and below the slide 50 mounted on the slide receiving members 152. In this manner, all of the fluid within each receptacle may be removed by tilting or disposing the case 73 vertically with the front wall 130 being positioned in a downward facing direction or by applying a vacuum or suction force to the outlet port 180 to draw all the fluid from the receptacle (separation mechanism). In this manner, the slide 50 in each individual receptacle in the case 73 may be individually washed so as to remove all traces of unreacted probe from the tissue 52 mounted on the slide 50 without contaminating adjacent samples (column 11, lines 51+).

9. Claims 1-7, 17-18, 29-31, 45, 47, 49 and 52 are rejected under 35 U.S.C. 102(b) as being anticipated by Takeuchi, US 4,738,824.

Takeuchi discloses an automatic dyeing apparatus M for dyeing specimens such as tissue or cell has a casing 1, in the upper portion of which a horizontal main table 2 is provided for disposing regularly many vessels v, v, . . . v thereon, each containing a kind of liquid such as reagent and water for dyeing specimens. Each vessel v has an open top face through which a specimen cage 3 for supporting many pieces of slide glass with specimens is immersed into the reagent or water of each vessel v. On the upper face of the casing 1 is provided a specimen cage transporting mechanism T (separating

mechanism) for transporting specimen cages into the respective vessels v. The mechanism T has a first slide body 4 extending laterally over the vessels v arranged on the main table 2 and the first slide body 4 is moved in the longitudinal direction (X direction) of the casing 1 while its opposite ends slide on respective guide rails 5, 5. Further, the first slide body 4 has a second slide body 6 extending vertically which is moved along the first slide body 4 in the lateral direction (Y direction) of the casing 1. The second slide body 6 has a support head 7 for supporting a specimen cage and the support head 7 is moved vertically along the second slide body 6 in the vertical direction (Z direction). The two slide bodies 4, 6 have two slits 4a, 6a formed on one side wall of their respective casings and one end of the first slide body 4 is moved along a slit 8a provided in an upper casing 8 which is formed on the back side of the upper portion of the casing 1. The casing 1 accommodates a plurality of reagent tanks 9a, 9b, . . . , 9e at its bottom (column 2, lines 21+).

In both groups, 1 and 2, the vessels have two inlets 23, 24, respectively, through which xylene in a tank 9a is supplied into the respective via a pump 25, two valves 26, 26 and two nozzles 27, 27 for adjusting flow rate of xylene. The vessels have two outlets 28, 28 for discharging used xylene.

In case that a plurality of dyeing reagents are used, a washing process must be carried out between the immersions of a dyeing reagent and a next dyeing reagent. After the specimen is dyed in the dyeing reagent, the specimen is washed by the normal water and/or the distilled water.

Claim Rejections - 35 USC § 103

10. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

11. Claims 11-15, 37-45, 49, and 52 are rejected under 35 U.S.C. 103(a) as being unpatentable over McGrath et al.

McGrath et al. does not disclose the device as including a temperature controller for heating and cooling.

McGrath et al. does teach A probe denoted by reference number 40 is releasably applied to the raised surface 14 on the mixing chamber surface 34 of the plate shown in FIG. 1 by suitable means, such as freeze -drying, etc. The probe 40 comprises any suitable antibody or nucleic acid used for reacting with tissue sections to mark and bind with message RNA or protein in a tissue section or cell to identify and quantify the macromolecule in the tissue section for subsequent analysis. By way of example, the probe 40 may be freeze-dried on the mixing chamber surface 34 in a 10 ul drop which can be efficiently re-wetted and released from the surface 34 so as to mix with a reactant fluid or blocking buffer, as described hereafter. Thus, the probe 40 is placed on the probe clip 10 in a dry, rewettable state. This allows the probe clip 10 to be prepared in advance for interchangeable use with tissue sections in performing in situ assays of such tissue sections. A probe denoted by reference number 40 is releasably applied to the raised surface 14 on the mixing chamber surface 34 of the plate shown in FIG. 1 by suitable means, such as freeze -drying, etc. The probe 40 comprises any suitable antibody or nucleic acid used for reacting with tissue sections to mark and bind with

message RNA or protein in a tissue section or cell to identify and quantify the macromolecule in the tissue section for subsequent analysis. By way of example, the probe 40 may be freeze-dried on the mixing chamber surface 34 in a 10 ul drop which can be efficiently re-wetted and released from the surface 34 so as to mix with a reactant fluid or blocking buffer, as described hereafter. Thus, the probe 40 is placed on the probe clip 10 in a dry, rewettable state. This allows the probe clip 10 to be prepared in advance for interchangeable use with tissue sections in performing in situ assays of such tissue sections.

It would have been obvious to one of ordinary skill in the art at the time of the invention to recognize the device maybe modified to include a temperature controller device to achieve the freezing and incubation of the slides as required by the method disclosed by McGrath et al.

As to the wedge and flexible members, McGrath et al. further states it would also be desirable to provide an in situ assay apparatus in which the reaction chamber has sufficient vertical space between a cover slide and the tissue carrying slide to reduce friction for complete reactant mixing.

After the completion of primary incubation, the tensioning means is released so as to enable the probe clip cassette 70 to move to a first position spacing the individual probe clips 10 from their corresponding slides 50.

It would have been obvious to one of ordinary skill in the art at the time of the invention to recognize wedges may be employed within the device of McGrath et al. in order to achieve the desired vertical space. It would further been obvious to one

ordinary skill in the art to recognize the automated device may be incorporated into a network including computers which may be employed for data storage, analysis, and subsequent transmission of such data.

Allowable Subject Matter

12. Claims 9, 33-34, 46, 50, 53 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

13. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian R. Gordon whose telephone number is 571-272-1258. The examiner can normally be reached on M-F, 1st Fri. Off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill Warden can be reached on 571-272-1267. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Brian R Gordon/
Primary Examiner
Art Unit 1797

brg